

C involve splice sites 5' to the start codon so that both splice variants encode the same iPLA_{2γ} polypeptide. Splice variant gamma 3, however, utilizes a start codon 5' to that of gamma 1 and gamma 2 to encode a longer polypeptide. SEQ ID NO:2. constitutes the cDNA of the coding region and SEQ ID NO: 1 constitutes the encoded polypeptide of alternative splice variants gamma 1 and gamma 2. SEQ ID NO:5 constitutes the cDNA of the coding region of splice variant gamma 3 and SEQ ID NO:2 constitutes the encoded polypeptide. ↘

Replace the last paragraph beginning at the bottom of page 4 and continuing to page 5 with the following paragraph.

C2 → The present invention is also directed to iPLA_{2γ} polynucleotides and fragments thereof which specifically hybridize under stringent conditions to the complements of the coding regions of iPLA_{2γ} polynucleotides set forth in SEQ ID NO:5 and the corresponding complement. In another aspect of this embodiment, the present invention is directed to iPLA_{2γ} polynucleotides comprising polynucleotides having at least about 90% identity with SEQ ID NO:2, and, preferably, such polynucleotides comprise SEQ ID NO:2. ↘

Replace the 2nd full paragraph beginning on page 4 and continuing to page 5 with the following paragraph.

C3 → In another aspect of this embodiment, the present invention is also directed to vectors and cells comprising a polynucleotide encoding an iPLA_{2γ} polynucleotide. In addition, the present invention encompasses antisense compounds which specifically hybridize to SEQ ID NO: 2. ↘

Replace the third full paragraph on page 5 with the following paragraph.

C4 → In a particular aspect of this embodiment, the present invention is directed to a fragment of an iPLA_{2γ} polynucleotide comprising an iPLA_{2γ} repressor binding site. Preferably, the polynucleotide comprises SEQ ID NO:3, 5'-TGATTTACGTTTAGCTCAATT-3'. ↘

Replace the third paragraph on page 5 with the following paragraph.

CS → In another embodiment, the present invention is directed to an isolated polypeptide comprising a phospholipase A_{2γ}. The isolated polypeptide catalyzes cleavage of fatty acids from the *sn*-2-position of phospholipids. In one aspect of this embodiment, the polypeptide has at least about 90% identity with SEQ ID NO:1; and, more preferably, the polypeptide comprises SEQ ID NO:1. In another aspect of this embodiment, the present invention comprises a conservatively substituted variant of SEQ ID NO:1. The present invention also encompasses antibodies capable of binding to a phospholipase A_{2γ} polypeptide. ↘

Replace the last paragraph on page 5 with the following paragraph.

Ch → Another embodiment of the present invention constitutes a method of treating inflammation in a patient. The method comprises treating the patient in need of such treatment to decrease calcium-independent phospholipase A_{2γ} activity in the patient. It is contemplated that patients in need of such treatment include those patients suffering from Alzheimer's disease, myocardial ischemia, or myocardial infarction. Preferably, the method comprises administering to the patient a phospholipase A_{2γ} translational repressor molecule. In another aspect of this invention, the method also comprises administering to the patient an antisense sequence which specifically hybridizes to SEQ ID NO:2. ↘

Replace the third paragraph on page 6 with the following paragraph.

C2 ↘ The present invention is also directed to an assay method for identifying substances which modulate iPLA_{2γ} expression in a cell. The method comprises contacting a candidate substance with cells comprising a promoter sequence operably linked to an iPLA_{2γ} repressor binding site and a reporter gene and measuring expression of the reporter gene. By iPLA_{2γ} repressor binding site it is meant that portion of the nucleotide sequence of an iPLA_{2γ} polynucleotide to which one or more endogenous substances within a cell bind to regulate translation of that iPLA_{2γ} polynucleotide.

C7
Preferably, the iPLA_{2γ} repressor binding site comprises SEQ ID NO:7. The reporter gene preferably encodes an enzyme capable of being detected by a colorimetric, fluorimetric or luminometric assay such as, for example, a reporter sequence encoding a luciferase. In a particularly preferred embodiment, the promoter sequence is a baculovirus promoter sequence and the cells are Sf9 cells. ~\

Replace the first paragraph on page 7 in the BRIEF DESCRIPTION OF THE DRAWINGS with the following paragraph.

C8
~\ Figure 1 shows the iPLA_{2γ} cDNA sequence (SEQ ID NO:4) which contains the coding region for the 88kDa iPLA_{2γ} polypeptide along with the corresponding amino acid sequence (SEQ ID NO:5). ~\

Replace the second paragraph on page 7 in the BRIEF DESCRIPTION OF THE DRAWINGS with the following paragraph.

C9
~\ Figure 2 illustrates three alternative splice variants of the iPLA_{2γ} gene. ~\

Replace the first-four paragraphs on page 8 with the following four paragraphs.

~\ Figure 3 illustrates the 5' portion of three alternative splice variants, identified as 1 (SEQ ID NO:6), 2 (SEQ ID NO:7) and 3 (SEQ ID NO:8) along with amino terminal portion of the encoded polypeptides corresponding to splice variants 1 and 2 (SEQ ID NO:9) and splice variant 3 (SEQ ID NO:10).

Figure 4 illustrates the full-length 88kDa polypeptide (SEQ ID NO:1) and the cDNA encoding the polypeptide (SEQ ID NO:2) along with sense primer, M444 (SEQ ID NO:11) and reverse primer, M458 (SEQ ID NO:12) used in the PCR amplification of the 88kDa polypeptide.

C10
Figure 5 illustrates the 77kDa truncated polypeptide starting at amino acid 101 and nucleotide 301 (SEQ ID NO:17) and the cDNA encoding the polypeptide (SEQ ID NO: 14) along with sense primer, m534 (SEQ ID NO: 15) and reverse primer, M458 (SEQ ID NO:16) used in the PCR amplification of the 74kDa polypeptide.

Figure 6 illustrates the 74kDa truncated polypeptide starting at amino acid 122 and nucleotide 364 (SEQ ID NO:17) and the cDNA encoding the polypeptide (SEQ ID NO:18) along with sense primer, m533 (SEQ ID NO:19) and reverse primer, M458 (SEQ ID NO:20) used in the PCR amplification of the 74kDa polypeptide.

Figure 7 illustrates the 63kDa truncated polypeptide starting at amino acid 221 and nucleotide 661 (SEQ ID NO:21) and the cDNA encoding the polypeptide (SEQ ID NO:22) along with sense primer, m530 (SEQ ID NO:23) and reverse primer, M458 (SEQ ID NO:24) used in the PCR amplification of the 74kDa polypeptide. ✓

C10
Replace the third paragraph on page 10 with the following paragraph.

-- Reference to iPLA_{2γ} or iPLA_{2γ} polypeptides herein is intended to be construed to include the polypeptides corresponding to coding regions of three spliced variants identified herein. The amino acid sequences of the polypeptides are as set forth in SEQ ID NO:1. The coding portion of the cDNA of the splice variants are as set forth in SEQ ID NO:2 (splice variants gamma 1 and gamma 2) and splice variant gamma 3 (see Figures 2-4). The iPLA_{2γ} polypeptides within the present invention are also intended to include iPLA_{2γ} of any origin which are substantially identical to and which are biologically equivalent to the iPLA_{2γ} polypeptides characterized and described herein. Such substantially identical iPLA_{2γ} may be native to any tissue or species and, similarly, biological activity can be characterized in any of a number of biological assay systems. The term "biologically equivalent" is intended to mean that the compositions of the present invention are capable of demonstrating some or all of the same *sn*-2-lipase activity, membrane localization and sensitivity to BEL inhibition, however, not necessarily to the same degree as the iPLA_{2γ} isolated herein as described in the examples below. ✓

C11
Replace the second paragraph on page 11 with the following paragraph.

C12
✓- Polypeptides considered to be included within the term iPLA_{2γ} polypeptides also includes conservatively substituted variants of SEQ ID NO:1 or SEQ ID NO:2.

C12

Conservative amino acid substitutions refer to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine; a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulfur-containing side chains is cysteine and methionine. Preferred conservative amino acids substitution groups include: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, and asparagine-glutamine, glutamic acid-aspartic acid, leucine-methionine; glutamine-histidine. ↘

Replace the third paragraph on page 11 with the following paragraph.

C13

↘ The iPLA_{2γ} polynucleotides of the present invention include those nucleic acid molecules, both DNA and RNA, which encode the iPLA_{2γ} polypeptides. Such iPLA_{2γ} polypeptides include, in particular, the coding regions of splice variants as set forth in SEQ ID NO:2 (splice variants gamma 1 and gamma 2) and splice variant gamma 3 (see Figures 2-4) as well as their complements. Also included are cDNA sequences which show at least 20% identity with the cDNA sequences defined above and sequences which hybridize. ↘

IN THE CLAIMS

C14

3. (once amended) An isolated nucleic acid molecule according to claim 2 wherein said polynucleotide encodes a sequence as set forth in SEQ ID NO: 1.

C15

6. (once amended) An isolated nucleic acid molecule comprising a fragment of a polynucleotide encoding a phospholipase A_{2γ} wherein said fragment specifically hybridizes with a sequence as set forth in SEQ ID NO: 1. AR not data